Do we need combination therapy?

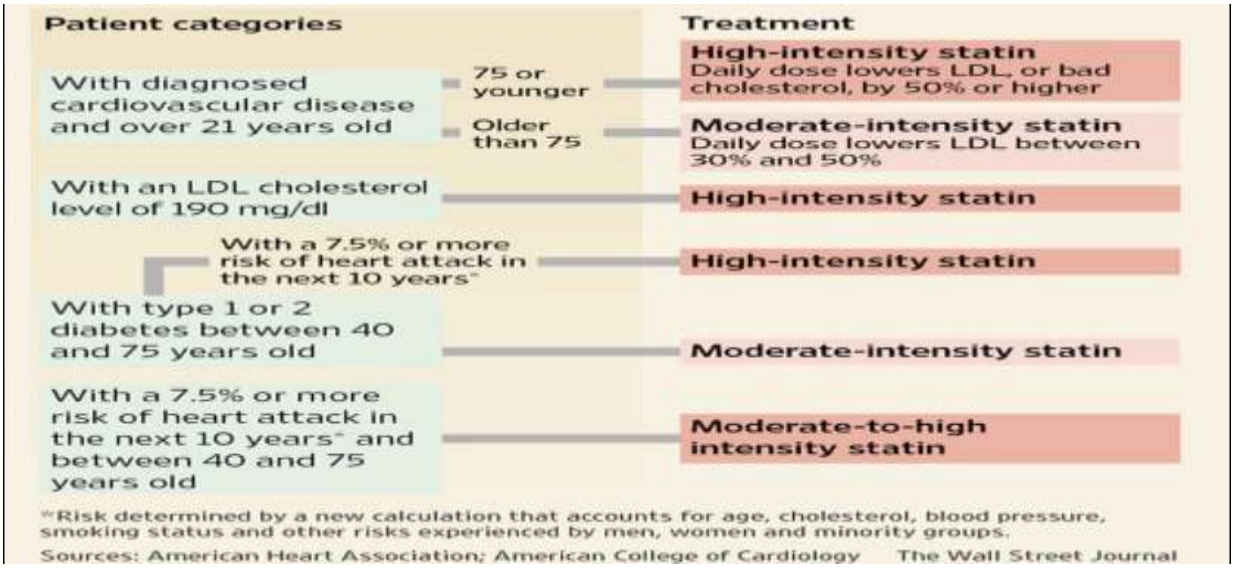
By
Ashraf Reda, MD, PhD, FESC
Prof. of Cardiology, Menofiya University
President of EAVA
EAVA
Director of the Egyptian Cardiorisk project

Case

- 54 yrs male smoker
- Type 2 DM on oral therapy
- MSCT showed non obstructive plaques LAD and LCX
- On Atorvastatin 40 mg/d
- Presented in your clinic worried about his dyslipidemia
- Recent lipid profile Showed LDL to be 68 mg/dl (1.6 mmol)

- What should we tell him?

American guidelines : 2013 ACC/AHA



ESC CP Guidelines 2016 – Highlights: Dyslipidaemias

Treatment targets

2011 ESC Dyslipidaemias guidelines

Recommendation	Class	Level
VERY-HIGH CV risk: LDL-c goal <70 mg/dl (1.8 mmol/L) and/or 50% reduction when target cannot be reached	I	A
HIGH CV risk: LDL-c goal <100 mg/l (2.5 mmol/L)	IIa	A
MODERATE CV risk: LDL-c goal <115 mg/dl (3.0 mmol/L)	IIa	C

2016 ESC Dyslipidaemias guidelines

Recommendation	Class	Level
VERY-HIGH CV risk: LDL-c goal <70 mg/dl (1.8 mmol/L) and/or 50% reduction if baseline is 70-135 mg/dl (1.8-3.5 mmol/L)	I	B
HIGH CV risk: LDL-c goal <100 mg/l (2.6 mmol/L) or 50% reduction if baseline is 100-200 mg/dl (2.6-5.1 mmol/L)	I	B
MODERATE CV risk: LDL-c goal <115 mg/dl (3.0 mmol/L)	IIa	C

ESC CONGRESS ROME 2016 #esccongress www.escardio.org/ESC2016

Case (cont…)

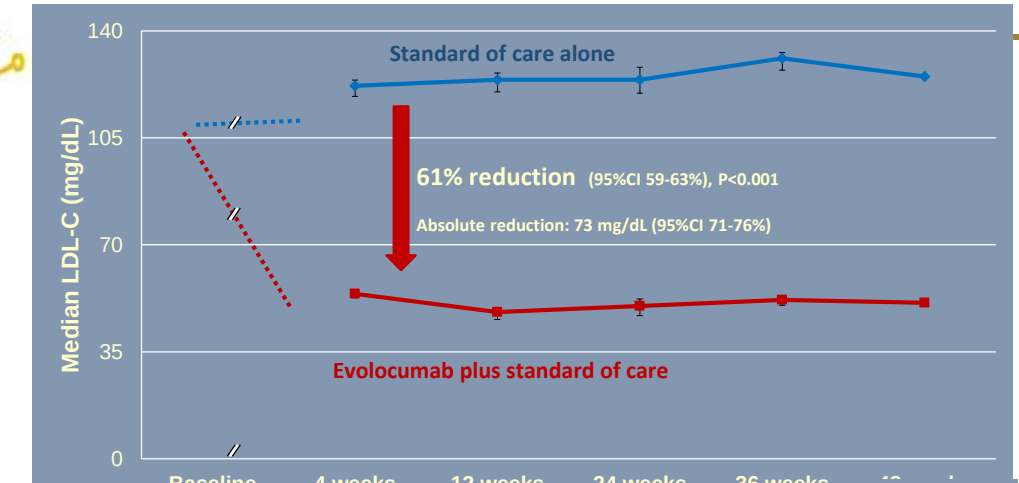
- His file revealed a base line LDL-c level of 102 mg/dl
- Q: are you still satisfactory with the treatment and LDL-c achieved?
- If not what are the options we have?

IMPROVE-IT

- 18.144 patients (ACS)
- Simva. 40 +Ezetimibe 10 Vs Simva 40 +placebo
- **53.2 mg/dl Vs 69.9 mg/dl** @ 1 year
- 32.7% primary end points VS 34.7% @ 7 yrs

- ***Suggesting that reduction of LDL-C levels per se explains the effects of statin on CAD***

LDL Cholesterol



	(Parent study)	(OSLER)			
	N=4465	N=1258	N=4259	N=4204	N=1243	N=3727
Abs. reduction (mg/dL)	60.4	73.4	70.4	72.7	70.5
Abs. reduction (mmol/L)	1.56	1.90	1.82	1.88	1.82

The dashed line indicate that patients were receiving either evolocumab or placebo during the period from baseline to enrollment into OSLER.

44y Female with Dyslipidemia.

- Dyslipidemic since she was 18y age.
- Grandfather died with STEMI by the age of 52.
- Father had Acute Coronary Syndrome by the age of 48.

Current treatment regimen:

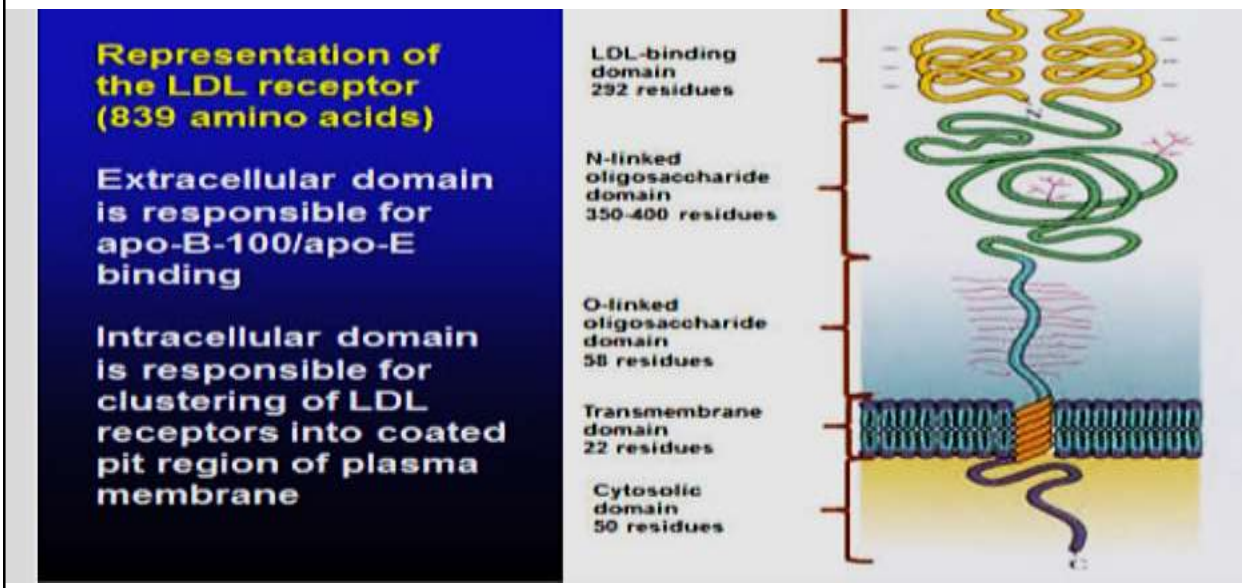
- Rosuvastatin 40mg (max tolerated dose)
- Ezetemibe 10 mg.

BMI: Body Mass Index;

On: Rosuvastatin 40mg and Ezetemibe 10mg

Now,
Her Lipid Profile:

Total Cholesterol	**290**
High Density Lipoprotein (HDL)	42
Triglycerides (TG)	190
Low Density Lipoprotein (LDL)	210



Egyptian Cardiorisk project

- The first Egyptian risk factor project with online data collection and electronic CRF
- Connecting > 28 CCUs
- Phase published in ESA 2017 .


CERTIFICATE OF PRESENTATION

THIS IS TO CERTIFY THAT

W. HAMED, A. RIDA, A. EL-KERSH, A. SHALABY, M. BISHAY

PRESENTED AN ABSTRACT ENTITLED

PRELIMINARY RESULTS OF THE EGYPTIAN CARDIOVASCULAR RISK FACTORS PROJECT:MULTICENTER OBSERVATIONAL STUDY OF THE PATTERN OF RISK FACTOR PROFILE IN EGYPTIAN PATIENTS WITH ACUTE CORONARY SYNDROME

DURING THE 84TH EAS CONGRESS

HELD ON

MAY 29- JUNE 1, 2016 IN INNSBRUCK, AUSTRIA

EAS 2016 CONGRESS SECRETARIAT

- Mean Age of onset of ACS in the Egyptian is 10-12 yrs less than European data

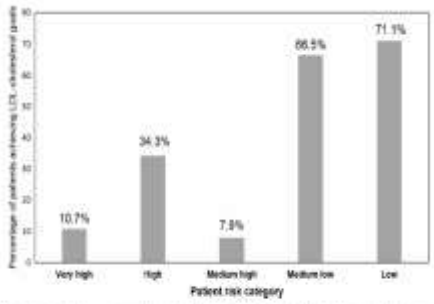


Fig. 4 Patient baseline risk category according to the NCEP ATP III 2004 updated guidelines obtaining their treatment goals. *NCEP ATP III* US National Cholesterol Education Program Adult Treatment Panel III guidelines

Only 11% of high risk Egyptian Pts is @ LDL-c goal


Springer for Research & Development

Home • Contact Us

EAVA

Centralized Pan-Middle East Survey on the Under-Treatment of Hypercholesterolemia: Results from the CEPHEUS Study in Egypt

A. Reda, A. A. Abdel-Rehim, A. Elmahi, O. S. A. Alfi

Download PDF (417 KB)

View Article

Look Inside

Adis

Other actions

Statin hypothesis Vs Lipid hypothesis

- The lower the better: 50 mg/dl better than 70 mg/dl in IMPROVE-IT
- Combination therapy is working
- PCSK-9 data
- Side effects and economic concerns

Pooled Safety LDL-C <25 mg/dL or <15 mg/dL in 14 Randomized, Controlled, Clinical Trials of Alirocumab

Primary system organ class, % (n) Preferred term, % (n)	Pooled control (n=1894)	Pooled alirocumab (n=3340)	Pooled alirocumab ≥2 LDL-C <25 mg/dL (n=796)	Pooled alirocumab ≥2 LDL-C <15 mg/dL (n=288)
Patients with any TEAE	**73.7** (1396)	**74.3** (2483)	**68.2** (543)	**67.0** (193)
Patients with any treatment emergent SAE	**13.3** (251)	**13.6** (453)	**13.1** (104)	**9.7** (28)
Patients with any TEAE leading to death	**1.0** (18)	**0.4** (15)	**0.4** (3)	**0** (0)
Patients with any TEAE leading to permanent treatment discontinuation	**6.6** (125)	**6.2** (207)	**3.5** (28)	**4.9** (14)

14

World Heart Federation
Strategic Principles for Development of National Clinical Guidelines

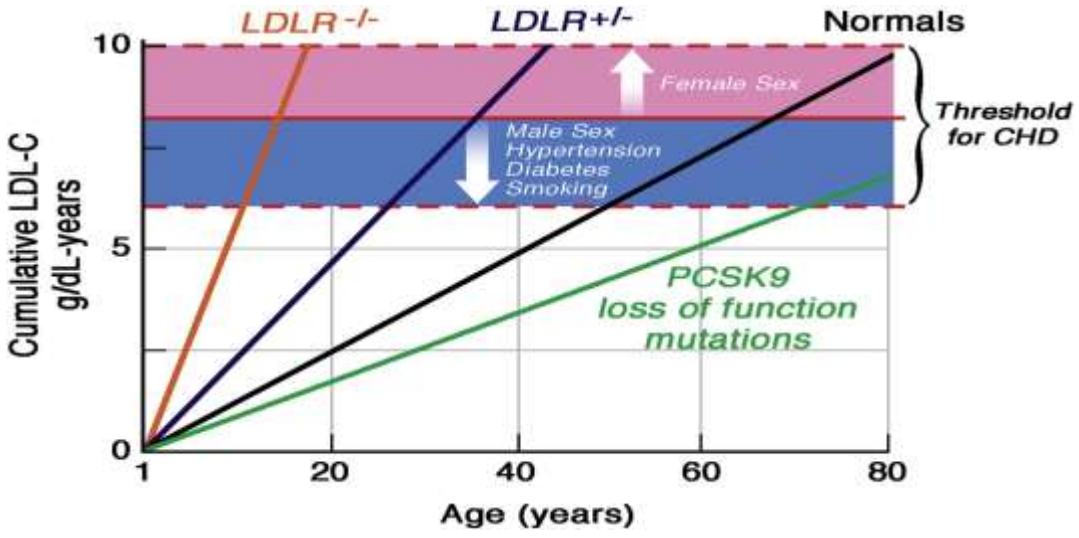
"Whereas the causes of CVD are common to all parts of the world, the approaches to its prevention at a societal or individual level will differ between countries for **cultural, social, medical, and economic reasons**."

Smith et al., Circulation June 29, 2004

IMPROVE-IT *

*presented AHA 2014

- A large scale (18,144 participants), multi-center RCT of high risk post **Acute Coronary Syndrome** (ACS) patients
- Intervention: ezetimibe 10 mg added to simvastatin 40*
- Comparator: simvastatin 40*
  Both groups achieved a mean LDL-C < 70 mg/dl
- Study took 9 years; f/u was 7 years
- No increase in side effects with the intervention
  *some uptitration allowed.


LDLR -/-
LDLR+/-
Normals
Female Sex
Male Sex
Hypertension
Diabetes
Smoking
Threshold for CHD
PCSK9 loss of function mutations
Cumulative LDL-C g/dL-years
10
5
0
1
20
40
60
80
Age (years)